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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/837,459	04/18/97	MCKEE M	4995.0023

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EXAMINER	
PORTNER, V	
ART UNIT	**PAPER NUMBER**
1645	27

DATE MAILED: 10/18/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/837,459	Applicant(s) McKee
	Examiner Portner	Group Art Unit 1645

☒ Responsive to communication(s) filed on *Jul 27, 2000* .

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *60, 64, and 65* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *60, 64, and 65* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 60, 64 and 65 are pending.

Claim 60 has been amended to recite a specific family of bacteria that produces intimin, specifically EHEC.

New Claims 64 and 65 have been added to define the type of antibodies administered, either polyclonal or monoclonal antibodies.

Rejections Maintained

1. Claims 60 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Cravioto et al (1991) as applied to claim 60, for reasons of record.

Please Note:

a.The examiner is reading the word "isolated" to mean separated from its native source and represents any degree of purity, obtained by any process of isolation and administered by any mode of administration, to include administration of colostrum to an infant by a mother, wherein the colostrum is administered orally to the patient (infant) in an isolated form. The composition administered need only comprise anti-intimin antibodies which is disclosed by Cravioto. Any other distinguishers have not been claimed.

b. Rejections withdrawn will not be addressed at this time.

Response to Arguments

2. Claims 60 and 65 rejected under 35 U.S.C. 102(b) as being anticipated by Cravioto et al (1991) is argued:

a. Cravioto et al does not utilize " isolated anti-intimin antibodies";

b.that the protective effect is due to the presence of many factors

c.and fails to indicate how a teaching of oligosaccharides, sIgA and other factors in breast milk would inherently lead to an administration of isolated anti-intimin antibodies providing a protective effect.

3. Applicant's arguments filed with respect to Cravioto et al (1991) have been fully considered but they are not persuasive because:

a. The colostrum upon administration was isolated from the mother and given to the child. The colostrum was no longer a part of the human body that produced it and was therefore isolated from the mother and given to the baby in an isolated form. No specific level of purity is recited in the claims, any level of purity is recited and must only be isolated from the source in which the antibodies were produced. No specific process steps are recited in the claim to define how the antibodies were obtained, therefore any method of obtaining isolated antibodies is claimed. Oral administration is not excluded by the claimed method as any mode of administration is encompassed by the scope of the claim.

b. The claimed invention recites open language and therefore permits the use of compositions that not only contain anti-intimin antibodies but compositions that contain other

components are permitted. Cravioto also discloses that the isolated antibodies blocked binding to a mammalian cell (see abstract, first sentence).

c. The inhibitory polyclonal antibodies were found to evidence prevention against infection in vivo in the patients to whom the antibodies were administered. Polyclonal antibodies are directed to the multiple epitopes present in a protein and therefore meets the claimed composition administered to a patient. The methods step of administration represents a process of introducing an isolated composition. The protective effect is protection from infection caused by E.coli strains that produce the attaching and effacing lesion mediated by intimin. Cravioto et al referred to intimin as the "adherence factor" (see abstract).

Agin et al, reference of record, quotes Cravioto as showing that sIgA isolated from human breast milk, blocks adherence of EPEC to Hep-2 mammalian cells (see page 318, paragraph 2) and that sIgA in breast milk recognized EPEC intimin (see page 318, first full paragraph lines 3-5). Agin also teaches that intimin is the bacterial protein that is required in the formation of attaching and effacing lesions characteristic of EPEC and EHEC infections in humans (abstract, first three lines). Protective polyclonal antibodies that are anti-intimin antibodies that are protective in EPEC would also inhibit binding of EHEC to mammalian cells. Inherently the anti-intimin polyclonal antibodies administered protected against the family of attaching and effacing lesion inducing pathogens, ~~entro~~entero hemorrhagic E.coli strains of bacteria are included in this family.

Inherently Cravioto et al disclose a method of providing passive immune protection comprising administering an amount of isolated anti-intimin antibodies effective to provide passive immune protection to a patient in need thereof and anticipates the now claimed invention.

New Claim Limitations/ New Grounds of Rejection

Claim Rejections - 35 U.S.C. § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Please Note: The following rejection is being made over the claim limitation "monoclonal antibodies" not previously recited in claim 60 which has received a first action on the merits made of record in paper number 24.

5. Claims 60 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dougan et al (US Pat. 5,747,293).

Dougan et al teach anti-intimin monoclonal antibodies for use in treatment of infection caused by E.coli linked with human diarrhoea (see col. 2, line 43 and col. 1, lines 8-11). The production of specific monoclonal antibodies to the carboxy-terminus of enteropathogenic and enterohemorrhagic E.coli intimin proteins (see col. 4, lines 6-7 (first full sentence)) is provided by

the invention. The antibodies taught are polyclonal and monoclonal antibodies and are useful in the treatment of infection (see col. 2, line 53 and col. 2, lines 47-52) . Treatment with monoclonal antibodies would be understood to be accomplished through administration of the monoclonal antibodies to a patient. Treating by definition results in blocking infection caused by the diarrhea causing pathogen, EHEC or EPEC, which produces intimin, wherein monoclonal antibodies to the carboxy terminal of intimin is taught to mediate attachment to patient cell receptors. The reference differs from the instantly claimed invention by failing to claim a method of passively protecting a patient through the administration of anti-intimin monoclonal antibodies.

In view of the prior art teaching EHEC intimin, teaching and suggesting the production of monoclonal antibodies and the use of monoclonal antibodies directed to intimin to block infection by treating a host, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to produce monoclonal antibodies to EHEC intimin for providing passive protection in a patient and to block the intimin domain that mediates receptor binding through the use of monoclonal antibodies that bind to the carboxy terminus of EHEC (see col. 2, lines 9-12) because monoclonal antibodies are known to provide for increased specificity of antigen binding, define a steady source of antibodies through hybridoma culture and are readily produced using well established biological methods.

The person of ordinary skill in the art would have been motivated by the reasonable expectation of success of obtaining monoclonal antibodies that block binding to a mammalian cell and would provide for passive protection of a patient because :

(1) Dougan et al teach screening methods for the isolation of specific monoclonals with the desired binding specificities;

(2) EHEC is known to produce human diarrhoea through the induction of an attaching and effacing lesion through the cooperation of intimin with other proteins (col.2, lines 10-17); and

(3) monoclonal antibodies that specifically bind to the intimin domain that mediates receptor binding would be useful in preventing the establishment of the attaching and effacing lesion that would result in passive protection through blocking of intimin interacting with patient receptors.

In the absence of a showing of unexpected results, Dougan et al teach the now claimed invention.

Conclusion

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

7. deAzavedo was previously cited to show that the C-terminal region of the attaching and effacing protein of EHEC is key to the process of binding to host patient receptors to cause infection and teaches that this domain carries the epitopes recognized by neutralizing monoclonal antibodies.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
October 16, 2000

L. F. Smith

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
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